THAT WHICH IS CLAIMED IS:

Replacing groups on oligos or substrate

1. A method for reducing non-specific binding of a target molecule to a plurality of oligonucleotides on a surface of a solid support, wherein said surface has a plurality of designated regions and a plurality of protected regions, each of said plurality of protected regions having a protecting group thereon, said method comprising:

a) producing said plurality of oligonucleotides at each of said designated regions, each of said plurality of oligonucleotides having a terminal protecting group; and

b) replacing with a negatively charged phosphate residue, at least one of:

i) the protecting groups on each of said plurality of oligonucleotides produced in step *a*), and

ii) the protecting groups on each of said plurality of protected regions; whereby non-specific binding of said target molecule is reduced.

2. The method according to Claim 1, wherein said solid support comprises polymerized Langmuir Blodgett film, functionalized glass, germanium, silicon, polymers, (poly)tetrafluoroethylene, polystyrene, gallium arsenide, metal oxide films, and combinations thereof.

3. The method according to Claim 1, wherein said step *a*) of producing said plurality of oligonucleotides comprises:

1) attaching to each of said designated regions an independently selected linker monomer having a photolabile protecting group;

2) attaching an independently selected nucleotide monomer having a photolabile protecting group to each of said attached linker monomers using light directed methods to produce a plurality of oligonucleotides having a terminal photolabile protecting group; and

3) repeating step *2*) from 1 to 120 times, to attach subsequent nucleotide monomers to each of said oligonucleotides produced in step *2*) to produce a plurality of oligonucleotides having a terminal photolabile protecting group.

4. The method according to Claim 1, wherein said step *a*) of producing said plurality of oligonucleotides comprises:

1) attaching to each of said designated regions an independently selected linker monomer having a chemically-removable protecting group;

2) replacing each of said chemically-removable protecting groups on each of said attached linker monomers with a photolabile protecting group;

3) attaching an independently selected nucleotide monomer having a chemically-removable protecting group to each of said attached linker monomers using light-directed methods to produce a plurality of oligonucleotides having a terminal chemically-removable protecting group;

4) replacing each of said chemically-removable protecting groups on each of said oligonucleotides with a photolabile protecting group; and

5) repeating steps *3*) and *4*) from 1 to 120 times, to attach subsequent nucleotide monomers to each of said oligonucleotides produced in step *3*) to produce said plurality of oligonucleotides having a terminal chemically-removable protecting group.

5. The method according to Claim 1, wherein said step *a*) of producing said plurality of oligonucleotides comprises:

1) attaching to each of said designated regions an independently selected linker monomer having a chemically-removable protecting group;

2) forming an activation layer on said designated regions and said protected regions, said activation layer comprising:

i) a photoactive agent, said photoactive agent producing a catalyst when irradiated, and

ii) an autocatalytic agent, said autocatalytic agent generating a product that removes said chemically-removable protecting group when said autocatalytic agent is activated by said catalyst;

3) irradiating a portion of said activation layer overlying said designated regions to remove said chemically-removable protecting group on said linker monomer;

4) attaching an independently selected nucleotide monomer having a chemically-removable protecting group to each of said attached linker monomers, to produce a plurality of oligonucleotides having a terminal chemically-removable protecting group;

5) irradiating a portion of said activation layer overlying said designated regions to remove said chemically-removable protecting group on said oligonucleotides;

6) repeating steps *4*) and *5*) from 1 to 120 times, to attach subsequent nucleotide monomers to each of said oligonucleotides produced in step *4*) to produce said plurality of oligonucleotides having a terminal chemically-removable protecting group.

Replacing groups with compound

6. The method according to Claim 1, wherein said step *b*) of replacing comprises:

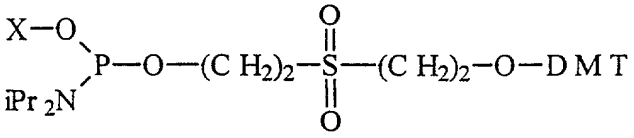
1) exposing at least one of: *i*) each of said plurality of oligonucleotides and *ii*) each of said plurality of protected regions, to an activator to remove the protecting groups, to produce activated sites; and

2) reacting said activated sites with a compound that covalently bonds a negatively charged phosphate residue to at least one of *i*) each of said plurality of oligonucleotides and *ii*) each of said plurality of protected regions.

7. The method according to Claim 6, wherein said protecting group is a photolabile protecting group and said activator is selected from the group consisting of ion beams, electron beams, gamma rays, x-rays, ultra-violet radiation, light, infra-red radiation, microwaves, electric currents, radiowaves, and combinations thereof.

8. The method according to Claim 6, wherein said protecting group is a chemically-removable protecting group and said activator is selected from the group consisting of acids, bases, oxidants, and reductants.

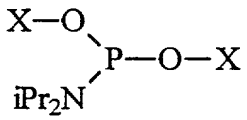
9. The method according to Claim 6, wherein said step *2*) of reacting said activated sites with a compound comprises reacting each of said activated sites with a compound selected from the group consisting of Formula I:



I

and

Formula II:



II

wherein:

DMT is a dimethoxy trityl protecting group;

each X is a base-removable protecting group; and

iPr_2N is diisopropyl amino protecting group.

Replacing groups by forming a polymer

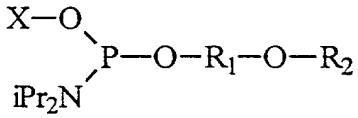
10. The method according to Claim 1, wherein said step *b*) of replacing comprises:

1) exposing at least one of: *i*) each of said plurality of oligonucleotides and *ii*) each of said plurality of protected regions, to an activator to remove the protecting groups to produce activated sites;

2) reacting said activated sites with a monomer having a negatively charged phosphate unit and a protecting group, whereby said monomer is covalently bound to at least one of *i*) each of said plurality of oligonucleotides and *ii*) each of said plurality of protected regions; and

3) repeating steps *1*) and *2*) from 1 to 20 times to produce a polyanion chain of negatively charged phosphate units on at least one of *i*) each of said plurality of oligonucleotides and *ii*) each of said plurality of protected regions.

11. The method according to Claim 10, wherein said step *2*) comprises reacting with a monomer of Formula III:



III

wherein:

R_1 is selected from the group consisting of a nucleoside moiety, a deoxyribose moiety, C_{1-8} alkylene, and $-(CH_2CH_2O)_m-$ wherein m is an integer from 1 to 8;

R_2 is a protecting group selected from the group consisting of a dimethoxy trityl protecting group and a MeNPOC protecting group;

X is a base-removable protecting group; and

iPr_2N is diisopropyl amino protecting group.

Replacing groups on both oligos & substrate

12. The method according to Claim 1, wherein said step *b*) of replacing comprises replacing both *i*) the protecting groups on each of said plurality of oligonucleotides produced in step *a*), and *ii*) the protecting groups on each of said plurality of protected regions.

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Coating oligos area with polymer

13. A method for reducing non-specific binding of a target molecule to a plurality of oligonucleotides on a surface of a solid support, wherein said surface has a plurality of designated regions and a plurality of protected regions, each of said plurality of protected regions having a protecting group thereon, said method comprising:

a) attaching a polyanion chain having a protecting group to each of said designated regions;

b) forming said plurality of oligonucleotides on each of said polyanion chains at each of said designated regions, each of said plurality of oligonucleotides having a terminal protecting group;

whereby non-specific binding of said target molecule is reduced.

14. The method according to Claim 13, wherein said solid support comprises polymerized Langmuir Blodgett film, functionalized glass, germanium, silicon, polymers, (poly)tetrafluoroethylene, polystyrene, gallium arsenide, metal oxide films, and combinations thereof.

Coating by forming polymer

15. The method according to Claim 13, wherein said step *a*) of attaching a polyanion chain comprises forming said polyanion chain on each of said protected regions, wherein said step of forming said polyanion chain comprises:

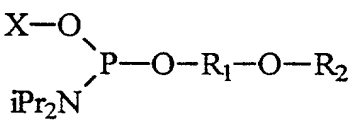
1) attaching a monomer to each of said designated regions, said monomer having a negatively charged phosphate unit and a protecting group, whereby said monomer is covalently bound to each of said designated regions;

2) exposing each of said monomers to an activator to remove the protecting group from each of said monomers to produce activated sites;

3) reacting said activated sites with said monomer having a negatively charged phosphate unit and a protecting group, to add a second monomer; and

4) repeating steps *2*) and *3*) from 0 to 20 times to produce a polyanion chain having a protecting group on each of said designated regions.

16. The method according to Claim 15, wherein said steps *1*) and *3*) comprise using a monomer of Formula III:



III

wherein:

R_1 is selected from the group consisting of a nucleoside moiety, a deoxyribose moiety, $C_{1\text{-}8}$ alkylene, and $-(CH_2CH_2O)_m-$ wherein m is an integer from 1 to 8;

R_2 is selected from the group consisting of a dimethoxy trityl protecting group and a MeNPOC protecting group;

X is a base-removable protecting group; and

iPr_2N is diisopropyl amino protecting group.

17. The method according to Claim 15, wherein said protecting groups are photolabile protecting groups and said step *2*) comprises using an activator selected from the group consisting of ion beams, electron beams, gamma rays, x-rays, ultra-violet radiation, light, infra-red radiation, microwaves, electric currents, radiowaves, and combinations thereof.

18. The method according to Claim 15, wherein said protecting groups are chemically-removable protecting groups and said step *2*) comprises using an activator selected from the group consisting of acids, bases, oxidants, and reductants.

Coating both oligos area & substrate with polymer

19. The method according to Claim 13, wherein said step *a*) of attaching a polyanion chain further comprises attaching a polyanion chain having a protecting group to each of said protected regions.

20. The method according to Claim 13, wherein said protecting groups comprise photolabile protecting groups and said step *b*) of forming said plurality of oligonucleotides comprises:

1) attaching an independently selected nucleotide monomer having a terminal photolabile protecting group to each of said polyanion chains at each of said designated regions using light directed methods;

2) repeating step *1*) from 1 to 120 times, to attach subsequent nucleotide monomers to each of said nucleotide monomers attached in step *1*) to produce a plurality of oligonucleotides having a terminal photolabile protecting group.

21. The method according to Claim 13, wherein said protecting groups comprise chemically-removable protecting groups and said step *b*) of forming said plurality of oligonucleotides comprises:

1) replacing each of said chemically-removable protecting groups on each of said attached polyanion chains at each of said designated regions with a photolabile protecting group;

2) attaching an independently selected nucleotide monomer having a chemically-removable protecting group to each of said attached polyanion chains using light-directed methods to produce a plurality of attached nucleotide monomers having a chemically-removable protecting group;

3) replacing each of said chemically-removable protecting groups on each of said nucleotide monomers with a photolabile protecting group;

4) attaching an independently selected nucleotide monomer having a chemically-removable protecting group to each of said attached nucleotide monomers using light directed methods to produce a plurality of oligonucleotides having a terminal chemically-removable protecting group;

5) repeating steps *3*) and *4*) from 1 to 120 times, to attach subsequent nucleotide monomers to each of said oligonucleotides produced in step *3*) to produce said plurality of oligonucleotides having a terminal chemically-removable protecting group.

22. The method according to Claim 13, wherein said protecting groups comprise chemically-removable protecting groups and said step *a*) of producing said plurality of oligonucleotides comprises:

1) forming an activation layer over said designated regions and said protected regions, said activation layer comprising:

i) a photoactive agent, said photoactive agent producing a catalyst when irradiated, and

ii) an autocatalytic agent, said autocatalytic agent generating a product that removes said chemically-removable protecting group when said autocatalytic agent is activated by said catalyst;

2) irradiating a portion of said activation layer overlying said designated regions to remove said chemically-removable protecting group on said polyanion chain;

3) attaching an independently selected nucleotide monomer to each of said attached polyanion chains at each of said designated regions, to produce a plurality of nucleotide monomers having a terminal chemically-removable protecting group;

4) irradiating a portion of said activation layer overlying said designated regions to remove said chemically-removable protecting group on each of said nucleotide monomers;

5) repeating steps *3*) and *4*) from 1 to 120 times, to attach subsequent nucleotide monomers to each of said nucleotides attached in step *3*) to produce said plurality of oligonucleotides having a terminal chemically-removable protecting group.

23. The method according to Claim 13, wherein said step *a*) of attaching a polyanion chain further comprises attaching a polyanion chain having a protecting group to each of said protected regions.

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Coating only substrate with polymer

24. A method for reducing non-specific binding of a target molecule to a plurality of oligonucleotides on a surface of a solid support, wherein said surface has a plurality of designated regions and a plurality of protected regions, each of said plurality of protected regions having a protecting group thereon, said method comprising:

a) attaching a polyanion chain having a protecting group to each of said protected regions; and

b) forming said plurality of oligonucleotides at each of said designated regions, each of said plurality of oligonucleotides having a terminal protecting group;

whereby non-specific binding of said target molecule is reduced.

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Coating oligos area with polymer & removing groups from oligos or substrate

25. A method for reducing non-specific binding of a target molecule to a plurality of oligonucleotides on a surface of a solid support, wherein said surface has a plurality of designated regions and a plurality of protected regions, each of said plurality of protected regions having a protecting group thereon, said method comprising:

a) attaching a polyanion chain having a protecting group to each of said designated regions;

b) forming said plurality of oligonucleotides on said polyanion chains at each of said designated regions, each of said plurality of oligonucleotides having a terminal protecting group; and

c) removing at least one of:

i) the protecting groups on each of said plurality of oligonucleotides produced in step *b*), and

ii) the protecting groups on each said plurality of protected regions;

whereby non-specific binding of said target molecule is reduced.

Coating oligos area with polymer & removing groups from both oligos & substrate

26. The method according to Claim 25, wherein said step *c*) of removing comprises removing both *i)* the protecting groups on each of said plurality of oligonucleotides produced in step *b*), and *ii*) the protecting groups on each of said plurality of protected regions.

Coating both oligos and substrate with polymer and removing groups from either oligos or substrate

27. The method according to Claim 25, wherein said step *a*) of attaching a polyanion chain further comprises attaching a polyanion chain having a protecting group to each of said protected regions.

Coating both oligos and substrate with polymer & removing groups from both oligos & substrate

28. The method according to Claim 27, wherein said step *c*) of removing comprises removing both *i)* the protecting groups on each of said plurality of oligonucleotides produced in step *b*), and *ii*) the protecting groups on each of said plurality of polyanion chains attached to each of said protected regions.

Coating substrate with polymer & removing groups from oligos or substrate

29. A method for reducing non-specific binding of a target molecule to a plurality of oligonucleotides on a surface of a solid support, wherein said surface has a plurality of designated regions and a plurality of protected regions, each of said plurality of protected regions having a protecting group thereon, said method comprising:

a) attaching a polyanion chain having a protecting group to each of said protected regions;

b) forming said plurality of oligonucleotides at each of said designated regions, each of said plurality of oligonucleotides having a terminal protecting group; and

c) removing at least one of:

i) the protecting groups on each of said plurality of oligonucleotides produced in step *b*), and

ii) the protecting groups on each said plurality of polyanion chains attached to each of said protected regions;

whereby non-specific binding of said target molecule is reduced.

Coating substrate with polymer & removing groups from both oligos & substrate

30. The method according to Claim 29, wherein said step *c*) of removing comprises removing both *i)* the protecting groups on each of said plurality of oligonucleotides produced in step *b*), and *ii*) the protecting groups on each of said plurality of polyanion chains attached to each of said protected regions.

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Coating oligos area with polymer & replacing groups on oligos or substrate

31. A method for reducing non-specific binding of a target molecule to a plurality of oligonucleotides on a surface of a solid support, wherein said surface has a plurality of designated regions and a plurality of protected regions, each of said plurality of protected regions having a protecting group thereon, said method comprising:

a) attaching a polyanion chain having a protecting group to each of said designated regions;

b) forming said plurality of oligonucleotides on said polyanion chains at each of said designated regions, each of said plurality of oligonucleotides having a terminal protecting group; and

c) replacing with a negatively charged phosphate residue, at least one of:

i) the protecting groups on each of said plurality of oligonucleotides produced in step *b*), and

ii) the protecting groups on each said plurality of protected regions;

whereby non-specific binding of said target molecule is reduced.

Coating oligos area with polymer & replacing groups with compound

32. The method according to Claim 31, wherein said step *c*) of replacing comprises:

1) exposing at least one of: *i*) each of said plurality of oligonucleotides and *ii*) each of said plurality of protected regions, to an activator to remove the protecting groups to produce activated sites; and

2) reacting said activated sites with a compound that covalently bonds a negatively charged phosphate residue to at least one of *i*) each of said plurality of oligonucleotides and *ii*) each of said plurality of protected regions.

Coating oligos area with polymer & replacing groups on oligos by forming polymer

33. The method according to Claim 31, wherein said step *c*) of replacing comprises:

1) exposing at least one of: *i*) each of said plurality of oligonucleotides and *ii*) each of said plurality of protected regions, to an activator to remove the

protecting groups, to produce activated sites;

2) reacting said activated sites with a monomer having a negatively charged phosphate unit and a protecting group, whereby said monomer is covalently bound to at least one of: *i*) each of said plurality of oligonucleotides and *ii*) each of said plurality of protected regions; and

3) repeating steps *1*) and *2*) from 1 to 20 times to produce a polyanion chain of negatively charged phosphate units on at least one of: *i*) each of said plurality of oligonucleotides and *ii*) each of said plurality of protected regions.

Coating oligos area with polymer & replacing groups on both oligos & substrate

34. The method according to Claim 31, wherein said step *c*) of replacing comprises replacing both *i)* the protecting groups on each of said plurality of oligonucleotides produced in step *b*), and *ii*) the protecting groups on each of said plurality of protected regions, with a negatively charged phosphate residue.

Coating both oligos and substrate with polymer and replacing groups from either oligos or substrate

35. The method according to Claim 31, wherein said step *a*) of attaching a polyanion chain further comprises attaching a polyanion chain having a protecting group to each of said protected regions.

Coating both oligos and substrate with polymer & replacing groups from both oligos & substrate

36. The method according to Claim 35, wherein said step *c*) of replacing comprises replacing both *i)* said protecting groups on each of said plurality of oligonucleotides produced in step *b*), and *ii*) said protecting groups on each said plurality of polyanion chains attached to each of said protected regions, with a negatively charged phosphate residue.

Coating substrate only with polymer & replacing groups on oligos or polymer

37. A method for reducing non-specific binding of a target molecule to a plurality of oligonucleotides on a surface of a solid support, wherein said surface has a plurality of designated regions and a plurality of protected regions, each of said plurality of protected regions having a protecting group thereon, said method comprising:

a) attaching a polyanion chain having a protecting group to each of said protected regions;

b) forming said plurality of oligonucleotides at each of said designated regions, each of said plurality of oligonucleotides having a terminal protecting group; and

c) replacing with a negatively charged phosphate residue, at least one of:

i) the protecting groups on each of said plurality of oligonucleotides produced in step *b*), and

ii) the protecting groups on each said plurality of polyanion chains attached to each of said protected regions;

whereby non-specific binding of said target molecule is reduced.

Coating substrate with polymer & replacing groups on both oligos & polymer

38. The method according to Claim 37, wherein said step *c*) of replacing comprises replacing both *i)* said protecting groups on each of said plurality of oligonucleotides produced in step *b*), and *ii*) said protecting groups on each said plurality of polyanion chains attached to each of said protected regions, with a negatively charged phosphate residue.

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Substrate

39. A solid support for solid-phase synthesis comprising a surface having a plurality of designated regions and a plurality of protected regions, wherein a polyanion chain having a protecting group is attached to at least one of: *i*) each of said designated regions, and *ii*) each of said protected regions.

40. A solid support according to Claim 39, wherein a polyanion chain having a protecting group is attached to both *i*) each of said designated regions, and *ii*) each of said protected regions.

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Method for Screening

41. A method for screening a target molecule for hybridization to a plurality of oligonucleotides, said method comprising:

a) providing a solid support comprising a surface having a plurality of designated regions and a plurality of protected regions, wherein a polyanion chain having a protecting group is attached to at least one of: *i*) each of said designated regions, and *ii*) each of said protected regions, and wherein one of said plurality of oligonucleotides is at each of said plurality of designated regions, said oligonucleotide being attached to said polyanion chain when said polyanion chain is attached to each of said designated regions;

b) contacting said target molecule to said plurality of oligonucleotides; and

c) detecting hybridization of said target molecule to said plurality of oligonucleotides;

wherein said polyanion chain reduces non-specific binding of said target molecule to said plurality of oligonucleotides.

42. The method according to Claim 41, wherein said polyanion chain is attached to both *i*) each of said designated regions, and *ii*) each of said protected regions, and wherein each of said plurality of oligonucleotides is attached to said polyanion chain at each of said designated regions.